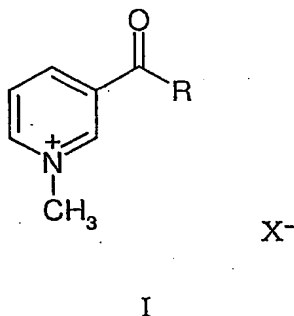


Claims

1. A use of quaternary pyridinium salts of the formula I:



5 wherein R is NH₂, CH₃, or N(H)CH₂OH group, and X is pharmaceutically acceptable counterion,

for the preparation of vasoprotective agent for the treatment or prevention of conditions or diseases associated with dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial prostacyclin PGI₂.

2. The use in accordance with claim 1, wherein said dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial prostacyclin PGI₂ coincides with hypercholesterolemia, hypertriglyceridemia or low HDL level.

15 3. The use in accordance with claim 1 or 2, wherein said condition or disease is atherosclerosis.

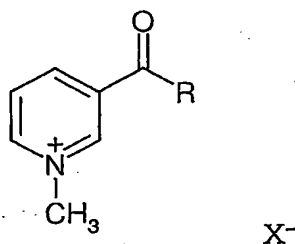
4. The use in accordance with claim 1 or 2, wherein said condition or disease is acute cardiovascular event associated with atherosclerosis, in particular sudden cardiac death, acute coronary syndrome (including unstable coronary artery disease, and myocardial infarct), the necessity of coronary angioplasty (PCI), coronary-aortal by-pass surgery (CABG), any type of surgery with extracorporeal circulation, ischemic stroke, or peripheral circulation revascularization.

25 5. The use in accordance with claim 1 or 2, wherein said condition or disease is atherosclerosis in patients with chronic coronary disease,

ischemic cerebrovascular episode or arteriosclerosis of the extremities, including thromboangitis obliterans.

- 5 6. The use in accordance with claim 1, wherein said condition or disease is selected from the group of risk factors for atherosclerosis, comprising the following: hypercholesterolemia, arterial hypertension, smoking, hyperhomocysteinaemia, insulin resistance, diabetes, menopause, aging, obesity, mental stress, infections, inflammatory states, including periodontal diseases, rheumatoid arthritis, allograft vasculopathy and nitrate tolerance.
- 10 7. The use in accordance with claim 1, wherein said condition or disease is dyslipidemia, in particular hypercholesterolemia or hypertriglyceridemia in particular associated with low plasma level of HDL.
- 15 8. The use in accordance with claim 1, wherein said condition or disease is thrombosis that is not related directly with atherosclerosis, in particular thrombosis associated with implantation of metallic vascular prostheses (stents), coronary-aortal by-pass surgery(CABG), hemodialysis, venous thrombo-embolic disease.
- 20 9. The use in accordance with claim 1, wherein said condition or disease is selected from the following group: chronic heart failure, pulmonary hypertension, microvascular diabetic complications, such as diabetic retinopathy and nephropathy, diabetic neuropathy, nephrotic syndrome, chronic renal failure, adults respiratory distress syndrome (ARDS), cystic fibrosis, chronic obstructive pulmonary disease (COPD), preeclampsia/eclampsia, erectile dysfunction, Stein-Leventhal syndrome, sleep apnea, systemic lupus erythematosus, sickle cell anemia, non-specific inflammatory bowel diseases, gastric or duodenal ulcers, glaucoma, chronic liver disease, primary amyloidosis, and neurodegenerative diseases.
- 25 10. The use in accordance with claim 9, wherein said condition or disease is chronic obstructive pulmonary disease.
- 30 11. The use in accordance with claim 9, wherein said condition or disease is chronic liver disease, in particular viral hepatitis.

12. The use in accordance with claim 9, wherein said neurodegenerative disease is selected from vascular dementia, Alzheimer's disease and Parkinson's disease.
13. The use in accordance with claim 9, wherein said disease is gastric or duodenal ulcer.
14. The use in accordance with any one of claims 1 to 13, wherein said vasoprotective agent is in a form for oral administration.
15. The use in accordance with any one of claims 1 to 13, wherein said vasoprotective agent is in a form for parenteral administration.
16. The use in accordance with any one of claims 1 to 13, wherein said vasoprotective agent is in a form for administration to the airways by inhalation.
17. The use in accordance with claim 10, wherein said condition or disease is chronic obstructive pulmonary disease and a medicament is in the form for inhalation administration.
18. The use in accordance with any one of claims 1 to 17, wherein R is CH₃ group.
19. The use in accordance with any one of claims 1 to 17, wherein R is NH₂ group.
20. The use in accordance with any one of claims 1 to 17, wherein R is N(H)CH₂OH group.
21. The use in accordance with claim 1 or 2, wherein said quaternary pyridinium salt is 1-methylnicotinamide salt and said condition or disease is hypercholesterolemia, hypertriglyceridemia or low HDL level.
22. A method for treatment or prevention of conditions or diseases associated with dysfunction of vascular endothelium, oxidative stress and insufficient production of endothelial PGI₂, comprising administration to a subject in a need thereof a therapeutically effective amount of a quaternary pyridinium salt of formula I:



wherein R is NH₂, CH₃, or N(H)CH₂OH group, and X is pharmaceutically acceptable counterion.

23. The method in accordance with claim 22, wherein said dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial prostacyclin PGI₂ coincides with hypercholesterolemia, hypertriglyceridemia or low HDL level.

24. The method in accordance with claim 22 or 23, wherein said condition or disease is atherosclerosis.

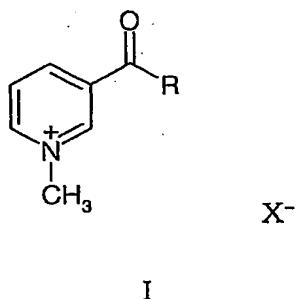
25. The method in accordance with claim 22 or 23, wherein said condition or disease is acute cardiovascular event associated with atherosclerosis, in particular sudden cardiac death, acute coronary syndrome (including unstable coronary artery disease, myocardial infarct), the necessity of coronary angioplasty (PCI), coronary-aortal by-pass surgery (CABG), ischemic stroke, or peripheral circulation revascularization.

26. The method in accordance with claim 22 or 23, wherein said condition or disease is atherosclerosis in patients with chronic coronary disease, ischemic cerebrovascular episode or atherosclerosis of the extremities, including thromboangitis obliterans.

27. The method in accordance with claim 22 or 23, wherein said condition or disease is selected from the group of risk factors for atherosclerosis, comprising the following: hypercholesterolemia, arterial hypertension, smoking, hyperhomocysteinaemia, insulin resistance, diabetes, menopause, aging, obesity, mental stress, infection- or inflammatory states, including periodontal diseases, rheumatoid arthritis, allograft vasculopathy or nitrate tolerance.

28. The method in accordance with claim 22 or 23, wherein said condition or disease is dyslipidemia, in particular hypercholesterolemia, hypertriglyceridemia in particular associated with low plasma level of HDL.
- 5 29. The method in accordance with claim 22 or 23, wherein condition or disease is thrombosis that is not related directly with atherosclerosis, in particular thrombosis associated with implantation of metallic vascular prostheses (stents), coronary-aortal by-pass surgery(CABG), any type of surgery with extracorporeal circulation, hemodialysis, venous thrombo-
10 embolic disease.
30. The method in accordance with claim 22 or 23, wherein said condition or disease is selected from the following group: chronic cardiac failure, pulmonary hypertension, microvascular diabetic complications, diabetic neuropathy, nephrotic syndrome, chronic renal failure, adults
15 respiratory distress syndrome (ARDS), cystic fibrosis, chronic obstructive pulmonary disease (COPD), preeclampsia/eclampsia, erectile dysfunction, Stein-Leventhal syndrome, sleep apnea, systemic lupus erythematosus, sickle cell anemia, non-specific inflammatory bowel diseases, gastric or duodenal ulcers, glaucoma, chronic liver disease, pri-
20 mary amyloidosis, neurodegenerative diseases.
31. The method in accordance with claim 30, wherein said neurodegenerative disease is selected from vascular dementia, Alzheimer's disease and Parkinson's disease.
32. The method in accordance with claim 30, wherein said disease is
25 gastric or duodenal ulcer.
33. The method in accordance with claim 30, wherein said condition or disease is chronic obstructive pulmonary disease.
34. The method in accordance with claim 30, wherein said condition or disease is chronic liver disease, in particular viral hepatitis.
- 30 35. The method in accordance with claim 22 or 23, wherein pyridinium salt of formula I is administered orally.

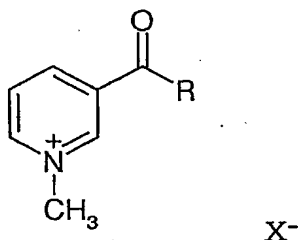
36. The method in accordance with claim 22 or 23, wherein pyridinium salt of formula I is administered parenterally.
37. The method in accordance with claim 22 or 23, wherein pyridinium salt of formula I is administered to the airways by inhalation.
- 5 38. The method in accordance with claim 22 or 23, wherein said condition or disease is chronic obstructive pulmonary disease and a medicament is in the form for inhalation administration.
39. The method in accordance with claim 22 or 23, wherein R is CH₃ group.
- 10 40. The method in accordance with claim 22 or 23, wherein R is NH₂ group.
41. The method in accordance with claim 22 or 23, wherein R is N(H)CH₂OH group.
42. The method in accordance with claim 22 or 23, wherein pyridinium derivative is administered together with cardiovascular agent.
- 15 43. The method in accordance with claim 22 or 23, wherein said quaternary pyridinium salt is 1-methylnicotinamide salt and said condition or disease is hypercholesterolemia, hypertriglyceridemia or low HDL level.
- 20 44. A method for enhancing a prostacyclin levels in mammals, which comprises oral administration of effective amount of quaternary pyridinium salt of formula I:



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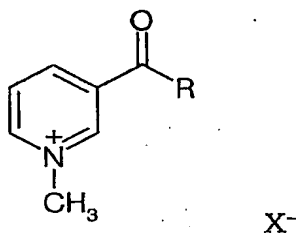
wherein R is NH₂, CH₃, or N(H)CH₂OH group, and X is pharmaceutically acceptable counterion.

45. Quaternary pyridinium salts of formula I:



wherein R is NH₂, CH₃, or N(H)CH₂OH group, and X is counterion acceptable for consumption, for use in oral diet supplementation.

46. A use of quaternary pyridinium salts of formula I:



wherein R is NH₂, CH₃, or N(H)CH₂OH group, and X is counterion acceptable for consumption, for the preparation of nutritional preparation for vascular protection in mammals in states or diseases associated with dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial prostacyclin (PGI₂)

47. The use in accordance with claim 46, wherein said dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial prostacyclin (PGI₂) coincides with hypercholesterolemia, hypertriglyceridemia and/or low HDL level.

48. The use in accordance with claim 46 or 47, wherein said condition or disease is atherosclerosis in patients with chronic coronary disease, ischemic cerebrovascular episode or arteriosclerosis of the extremities, including thromboangitis obliterans.

5 49. The use in accordance with claim 46 or 46, wherein said condition or disease is selected from the group of risk factors for atherosclerosis, comprising the following: hypercholesterolemia, arterial hypertension, smoking, hyperhomocysteinaemia, insulin resistance, diabetes, menopause, aging, obesity, mental stress, infection- or inflammatory
10 states, including periodontal diseases, reumatoid arthritis, allograft vasculopathy or nitrate tolerance.

50. The use in accordance with claim 46 or 47, wherein said condition or disease is dyslipidemia, in particular hypercholesterolemia, hypertriglyceridemia in particular associated with low HDL plasma level .

15 51. The use in accordance with claim 46 or 47, wherein condition or disease is thrombosis that is not related directly with atherosclerosis, in particular thrombosis associated with implantation of metallic vascular prostheses (stents), coronary-aortal by-pass surgery(CABG), any type of surgery with extracorporeal circulation, hemodialysis, venous thrombo-
20 embolic disease.

52. The use in accordance with claim 46, wherein insufficient production of endothelial prostacyclin is age-related.

53. The use in accordance with claims 46 to 52, wherein R is CH₃ group.

25 54. The use in accordance with claims 46 to 52, wherein R is NH₂ group.

55. The use in accordance with claims 46 to 52, wherein R is N(H)CH₂OH group.

30 56. The use in accordance with claim 46 to 52, wherein said quaternary pyridinium salt is 1-methylnicotinamide salt and said condition or disease is hypercholesterolemia, hypertriglyceridemia or low HDL level.